Homologous and Heterologous Venous Replacement with Synthetic Graft Covered with Canine Pseudointima

AUTHOR(S):

ONO, KEIJI

CITATION:

ONO, KEIJI. Homologous and Heterologous Venous Replacement with Synthetic Graft Covered with Canine Pseudointima. 日本外科宝函 1965, 34(6): 1462-1485

ISSUE DATE:

1965-11-01

URL:

http://hdl.handle.net/2433/206548

Homologous and Heterologous Venous Replacement with Synthetic Graft Covered with Canine Pseudointima

by

KEIJI ONO

From the 2nd Department of Surgery, Kyushu University Faculty of Medicine
(Director: Prof. KIYOSHI INOKUCHI)

Received for Publication Sept. 9, 1965

I. INTRODUCTION

Venous grafts are clinically desirable for large veins involved in obstruction, neoplastic invasion, congenital anomalies and extensive laceration. However, despite the satisfactory use of various prosthetic materials for arterial reconstruction, replacement of venous segments remains one of the unsolved problems in vascular surgery. Prosthetic grafts made from synthetic fibers were widely used experimentally and clinically but, in general, little success has been encountered[8]. While autologous vein is usually the choice of graft[4)8)], the available autologous veins are rarely of adequate caliber for use in the vena cava[1)]. Numerous variables may be responsible for the failure of venous grafts. However, they would seem to be related to two fundamental factors. First, the type of the graft employed appears to be of primary importance. Second, the low intraluminal pressure in venous channels. This second factor has been amply demonstrated by the observation that almost any type of graft remains patent for a considerable length of time when large arteries are concerned. It appears obvious that since the intraluminal pressure cannot be altered the graft must be modified to obtain a better result in venous surgery. The awareness of these facts has stimulated many investigators to experiment with graft of different materials in an attempt to find a suitable venous substitutes[8].

It has been recongnized that synthetic graft placed in the aorta is covered with pseudointima in several weeks and that such a graft remains patent[33)]. This evidence encouraged me to attempt to utilize graft whose inner surface was covered with pseudointima and consequently was as smooth as that of a blood vessel[12)]. If the transplantation of the pseudointima, which histologically has a rather simple structure, is possible in homologous and heterologous animals, it may contribute to the solution of the fundamental problems in organ transplantation, and also towards the development of new venous grafts. In the present study, crimped woven Tetoron graft* placed in the defect of canine abdominal aorta several weeks previously and covered with canine pseudointima was inserted into infra-renal vena cava in homologous (dog) and heterologous (cat) animals.

II. EXPERIMENTAL METHOD

The study was divided into four parts: (1) control venous grafting with Tetoron graft without pseudointima, (2) insertion of the Tetoron graft into the canine abdominal aorta,

(3) homologous venous grafting with Tetoron graft covered with canine pseudointima, (4) heterologous grafting in cats with Tetoron graft covered with canine pseudointima including patch grafting.

In this study 140 mongrel adult dogs and 35 adult cats of both sexes were used (Table 1). The procedures were performed under intravenous anesthesia with pentobarbital sodium (30 to 40 mg per kg body weight). All operations were performed under sterile condition. The procedures are described in detail subsequently. Heparinized saline solution was used for the irrigation of the graft, but no systemic heparinization was used either during or after any of the procedures. Synthetic graft were cut with scissors and in no instances were the end cauterized. Particular attention was paid to absolute hemostasis and careful wound management. Anastomosis was performed carefully so that neither adventitia nor the cut edge of a graft would be turned into the lumen to enhance thrombosis. Antibiotics were given either intramuscularly or intravenously for the first 2 to 3 days after the procedures and no dressing was applied. Anti-immunologic drugs were not used in any of the procedures. In some instances, venography was carried out. These were obtained by exposure of an x-ray film just at the completion of the rapid injection of 5 to 15 cc of 75% Urokolin** into the vein. Autopsy examinations were conducted at appropriate times. Carefully exposed, the segment of the transplant and adjoining proximal and distal vein was removed. It was fixed to a wooden plate, immersed in 10% formalin and embedded in paraffin. The cross and longitudinal sections were stained (1) with hematoxylin and eosin, (2) with van Gieson's stain, (3) with PAS stain, and (4) with Mallory's stain.

1. CONTROL GRAFTING WITH TETORON GRAFT WITHOUT PSEUDOINTIMA

a. Method

Five dogs varying in weight between 8 to 10 kg were used. Infra-renal vena cava was mobilized and a 1 cm long segment was excised. Crimped woven Tetoron graft without

Table 1 Summary of Experiments

	Graft	Position	Suturing	No.	Time Followed (days)
Homologous	Tetoron Graft Covered with Canine Pseudointima 7 to 10 mm in Diameter	I. V. C. (dog)	Apparatus suturing	6	7 to 445
			Manual suturing with 6-0 nylon	20	1 to 445
			Manual suturing with 6-0 silk	19	7 to 555
Heterologous	6 to 8 mm in Diameter	I. V. C. (cat)	Manual suturing with 6-0 nylon	29	1 to 56
	Patch Graft	I. V. C. (cat)	Manual suturing with 6-0 nylon	6	18 to 54
Control	Tetoron Graft 8 mm in Diameter	I. V. C. (dog)	Manual suturing with 6-0 silk	5	7 to 10
Modification of Graft	Tetoron Graft 6 to 10 mm in Diameter	Abdominal aorta (dog)	Apparatus suturing	90	22 to 135

Table 2 Summary of Control Venous Grafting with Tetoron Graft.

No.	Dog No.	Size of Graft (mm)	Time Followed (days)	Patency at Autopsy	Remarks
1	331	8×20	10	Occluded	Thrombosis
2	338	8×20	7	Occluded	Thrombosis
3	336	8×20	7	Occluded	Thrombosis
4	335	8×20	7	Occluded	Thrombosis
5	332	8×20	7	Occluded	Thrombosis

pseudointima, 2 cm long and 8 mm in diameter, was inserted into the defect of the vena cava. Anastomosis was completed with an over-and-over continuous suture of No. 6-0 silk.

b. Results

All animals survived operation. Vena cavograms taken 7 days after the operation revealed occlusions in 4 grafts and marked stenosis in 1 graft. This last graft was found to be occluded on the 10th postoperative day. Autopsy revealed all grafts to be entirely filled with thrombus (Table 2).

2. INSERTION OF TETORON GRAFT INTO CANINE ABDOMINAL AORTA (MODIFYING THE SYNTHETIC GRAFT IN VIVO)

a. Method

Resection and replacement of the abdominal aorta with crimped woven Tetoron graft was undertaken in 90 mongrel dogs, weighing 12 to 20 kg. The abdomen was entered through a midline incision in the lower abdominal wall. The intestines were packed upwards out of the pelvis and lower abdomen. The peritoneum was incised over the abdominal aorta from its trifurcation up to the origin of the renal arteries. Several pair of lumbar branches were ligated and the infra-renal abdominal aorta was freed from its surrounding connective tissue. A 1.0 cm long segment of aorta was resected and the crimped woven Tetoron graft, 4 to 5 cm in length and 6 to 10 mm in inner diameter, was inserted into the defect using INOKUCHI's blood-vessel-suturing-apparatus[13] (Fig. 1). The prosthesis was selected which had a diameter slightly larger than that of the host abdominal aorta. The proximal end was connected first and the graft was preclotted. This step greatly reduced blood loss from graft

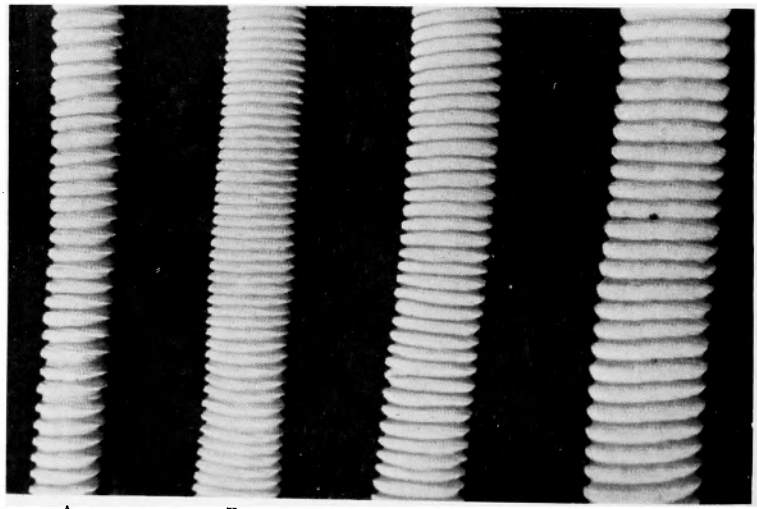


Fig. 1 Crimped woven Tetoron graft.
A: 6 mm, B: 7 mm, C: 8 mm, D: 10 mm in diameter.

mesh subsequently. The peritoneum was sutured loosely over the graft and the abdominal wound was closed. To determine the patency of the graft, palpable femoral pulses were substantiated daily for 1 week and then weekly. These grafts were removed 22 to 135 days after insertion and used as venous substitutes. At the removal of the graft, the region of the graft was mobilized and heparinized saline solution was injected into the graft immediately after applying occlusive clamps proximally and distally. After removal, the connective tissue around the graft 'pseudoadventitia' was peeled out. A segment of approximately 5 mm was cut from one end of the graft for pre-grafting histological study and the remainder was inserted into homologous and heterologous infra-renal vena cava.

b. Results

Palsy of the hind legs was seen within 2 days in 4 animals and the femoral pulse diminished or gradually obliterated without any evidence of weakness or palsy of the hind quarters in another 7 dogs. These animals were sacrificed and autopsy revealed that the grafts were occluded with thrombus. These early or late thrombi were seen in 3 of 6 grafts with 6 mm diameter, in 3 of 17 grafts with 7 mm diameter, and in 3 of 39 grafts with 8 mm diameter and were not encountered in the group with 10 mm graft. Five dogs died of distemper within 1 month and 1 expired with peritonitis on the third day. Three grafts were surrounded with peri-vascular hematoma. These grafts were not used bacause of insufficient coverage of pseudointima. The remaining 72 grafts were found to be patent and completely covered with smooth, fairly transparent pseudointima of variable thickness (Fig. 2). In general, the pseudointima was relatively thicker near the suture lines.

Histological findings after the insertion of the Tetoron graft into the canine abdominal aorta were as follows: The graft of 22 days was partly covered with a eosinophilic homogenous substance which was thought to be fibrin clot. Some fibroblasts and round cells were noted near the graft in the clot. On most of the internal surface of the graft, the fibrin clot was being replaced with young connective tissue containing large spindle-shaped fibroblasts and delicate fibrile (Fig. 3). After 29 days postoperatively, the remaining clot was minimal and the

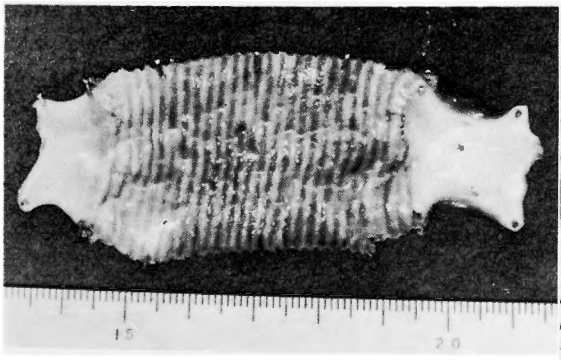


Fig. 2 Tetoron graft which was placed in canine abdominal aorta for 42 days and covered with canine pseudointima. Pseudointima is white and thick near suture lines.

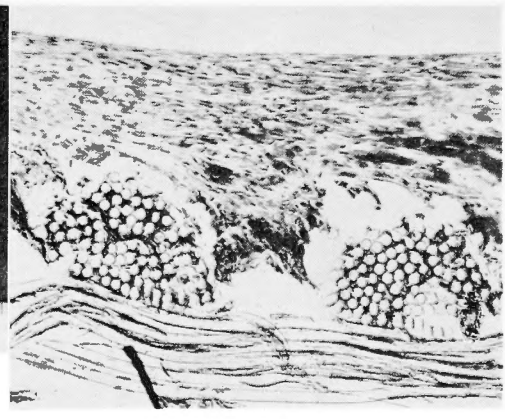


Fig. 3 Tetoron graft placed in canine abdominal aorta for 29 days, Fibrin clot has been partially replaced with collagenous connective tissue. Hematoxylin and eosin. ×118

fibroblasts and fibrocytes increased in number. The graft of 38 days was completely covered with young connective tissue and no clot remained. Collagenous fibers increased in number while connective tissue cells decreased proportionately in number. Collagenous fibers and fibroblasts were arranged longitudinally in the superficial portion and irregularly in the deeper portion. The graft was surrounded with matured connective tissue with slight infiltration of inflamatory infiltrate near the graft. The graft 58 days in age was covered with a thin collagenous layer with a few fibroblasts and fibrocytes, all arranged longitudinally. The graft was surrounded with thick connective tissue which was characterized by numerous collagenous bundles with accumulation of young connective tissue cells near the graft. Incorporation of the connective tissue in both sides of the graft was also noted. The graft of 90 days was covered with matured connective tissue comprised of many collagen bundles and a few connective tissue cells. Lymphocytic infiltration was seen outside of the graft (Fig. 4). Incorporation of the tissue in both sides of the graft was not remarkable. After 104 days postoperatively, the pseudointima of the graft mainly consisted of matured collagenous tissue arranged longitudinally. In the deeper portion, near the graft, hyalinization of the collagen bundles was noted and calcification was proceeding (Fig. 5). In the graft of 107 days, there was no evidence of calcification. The graft was covered with relatively matured connective tissue which was well incorporated into the tissue outside of this graft. After 135 days postoperatively, most collagenous bundles were hyalinized and inert. Necrosis was seen in small areas near the graft, but no evidence of calcification was encountered.

3. HOMOLOGOUS VENOUS REPLACEMENT WITH TETORON GRAFT COVERED WITH CANINE PSEUDOINTIMA

a. Method

Fourty five adult mongrel dogs varying in size from 8 to 12 kg were used. Infra-renal vena cava was exposed through a midline incision in the lower abdomen. Several lumbar veins were ligated and the inferior vena cava was freed from surrounding connective tissue.

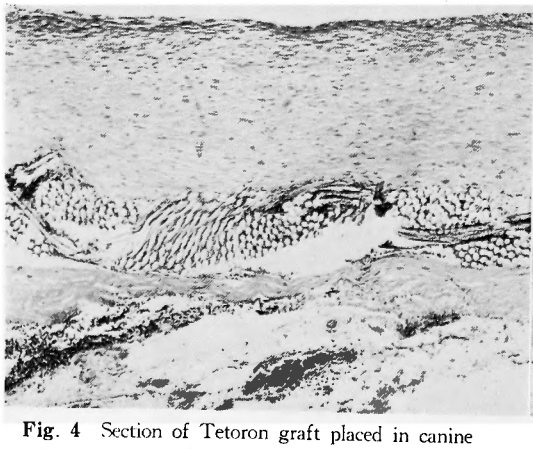


Fig. 4 Section of Tetoron graft placed in canine abdominal aorta for 90 days. The graft is covered with inert pseudointima, but lymphocyte infiltration is noted outside of the graft. Hematoxylin and eosin ×68

Fig. 5 Section of Tetoron graft placed in canine abdominal aorta for 104 days. Collagen bundles in deeper portion are hyalinized and calcification is noted. Hematoxylin and eosin. ×90

A 1 cm long segment of vena cava was resected between SATINSKI clamps. The resected caval segment was replaced with crimped woven Tetoron graft which had been placed in canine abdominal aorta for longer than 22 days and covered with pseudointima. The graft was selected so that the animal would receive isodiametric or slightly larger graft than the adjacent vena cava. Anastomosis was carried out by INOKUCHI's blood-vessel-suturing-apparatus in 6 dogs, by manual suturing with 6-0 silk in 19 dogs and with 6-0 nylon in 20 dogs. In the case of apparatus suturing, care was taken to neither injure nor detach the pseudointima from the graft. In the group having manual suturing, the anastomosis was completed with an over-and-over continuous suture after the placement of stay suture halfway about the circumference. After completion of the anastomosis the distal atraumatic clamp was released first to allow the displacement of air contained in the grafted segment. The proximal clamp was then removed and usually only minor bleeding occurred. If a significant leak was noted, it was closed with an additional suture. The graft appeared to function satisfactorily in all animals at the time of placement. The peritoneum was loosely sutured over the graft and the abdominal wound was closed in anatomical layers. Vena cavography was carried out at 1, 2, 5, 10, 15 weeks after grafting and thereafter at appropriate interval until complete occlusion was demonstrated. Animals with patent grafts were sacrificed at appropriate intervals for gross and histological study, while occluded graft was removed immediately after the demonstration of occlusion by cavogram.

b. Results

The death of 1 animal within 24 hours was attributed to anesthesia. Fourty four dogs survived operation and were followed up to 555 days (Table 3-A, B, C). Peripheral edema was not apparent in any dogs postoperatively, although the anterior abdominal veins frequently became prominent and suggested thrombosis. Twenty one grafts became occluded with thrombus formation. Periodical vena cavograms showed 13 occlusions after 7 days, 5 occlusions after 14 days, 1 occlusion after 21 days and 2 occlusions after 35 days postoperatively. No occlusion was seen after 35 days. Coincident with thrombosis in the graft, an extensive collateral system developed which was of a sufficient magnitude to prevent the occurrence of edema in the hind quarters. Thrombus filled the entire graft in all cases of occlusion and further extended to the distal adjacent host vein in 3 cases. Twenty three grafts were found to be patent for various periods up to 555 days, and the analyzed patency rate has been tabulated (Table 4). Inadvertent death occurred 14 days after grafting in 2 dogs during

Table 3-A Summary of Homologous Venous Grafting with Tetoron Graft Covered with Canine Pseudointima.

No.	Dog No.	Size of Graft (mm)	Growing Time of Pseudointima (days)	Time Followed (days)	Patency at Autopsy	Remarks
1	353	8×20	45	75	Patent	White smooth pseudointima
2	355	8×20	50	395	Patent	White smooth pseudointima
3	362	10×20	30	—	—	Died of anesthetic
4	363	8×20	40	7	Occluded	Thrombosis
5	364	8×20	43	445	Patent	White smooth pseudointima
6	368	8×20	36	35	Occluded	Thrombosis

Table 3-B Summary of Homologous Venous Grafting with Tetron Graft Covered with Canine Pseudointima (Manual suturing group with nylon)

No.	Dog No.	Size of Graft (mm)	Growing Time of Pseudointima (days)	Time Followed (days)	Patency at Autopsy	Remarks
1	351	8×20	45	50	Patent	Inner layer : partly red
2	352	8×20	48	372	Patent	White smooth pseudointima, slight constriction
3	354	10×20	45	410	Patent	Significant wrinkle of graft
4	356	8×20	53	14	Patent	Center of pseudointima : reddish
5	357	10×20	26	14	Occluded	Thrombosis
6	358	8×20	25	7	Occluded	Thrombosis
7	359	8×20	29	14	Occluded	Thrombosis
8	360	8×20	33	7	Occluded	Thrombosis
9	361	8×20	30	445	Patent	Smooth white pseudointima, slight stenosis
10	365	10×20	31	7	Occluded	Thrombosis
11	366	10×20	33	7	Occluded	Thrombosis
12	367	10×25	31	14	Occluded	Thrombosis
13	372	8×15	83	88	Patent	White smooth pseudointima, slight constriction
14	81	8×15	93	20	Patent	Center of pseudointima : red, near suture lines : white
15	84	8×15	93	35	Patent	White pseudointima
16	88	7×15	90	6	Patent	Inner layer : red
17	93	10×20	76	8	Patent	Inner layer : red and swollen
18	72	10×20	76	19	Patent	Center of pseudointima : red, near suture lines : white
19	379	10×20	104	1	Patent	Small coagulum adheres to inner layer
20	87	8×20	110	3	Patent	Small coagulum adheres to inner layer

Table 3-C Summary of Homologous Venous Grafting with Tetoron Graft Covered with Canine Pseudointima (Manual suturing group with silk)

No.	Dog No.	Size of Graft (mm)	Growing Time of Pseudointima (days)	Time Followed (days)	Patency at Autopsy	Remarks
1	324	8×20	42	555	Patent	Pseudointima : roundly defected constriction at suture lines
2	311	8×20	43	7	Occluded	Thrombosis
3	315	8×20	36	7	Occluded	Thrombosis
4	313	10×20	38	276	Patent	White smooth pseudointima, slight flattening
5	311	8×20	40	14	Patent	Died of anesthetic during venogram
6	342	8×20	39	14	Occluded	Thrombosis
7	343	8×25	39	7	Occluded	Thrombosis
8	344	10×20	42	7	Occluded	Thrombosis
9	345	10×20	31	538	Patent	White smooth pseudointima, slight constriction
10	340	10×20	33	471	Patent	White smooth pseudointima, minimal constriction
11	339	10×20	33	35	Occluded	Thrombosis
12	337	10×20	40	7	Occluded	Thrombosis
13	333	8×10	34	14	Occluded	Thrombosis
14	346	10×20	22	508	Patent	White smooth pseudointima, minimal constriction
15	317	10×20	24	7	Occluded	Thrombosis
16	348	8×20	36	7	Occluded	Thrombosis
17	349	10×20	26	7	Occluded	Thrombosis
18	350	10×20	31	21	Occluded	Thrombosis
19	95	7×10	94	28	Patent	Pseudointima : slightly red

Table 4 Periodical Patency Rate of Tetoron Graft Covered with Canine Pseudointima Placed in Homologous Inferior Vena Cava

Graft	No.	Suturing	1 wk.	2 wks.	5 wks.	10 wks.	15 wks.
		Total	29/42 69.0%	21/38 55.3%	14/35 40.0%	13/34 38.2%	10/31 32.3%
Tetoron Graft Covered with Canine Pseudointima	45***	Suturing Apparatus	4/5 80.0%	4/5 80.0%	3/5 60.0%	3/5 60.0%	2/4 50.0%
		Manual Suturing with 6-0 nylon	14/18 77.8%	8/14 57.1%	6/13 46.2%	5/12 41.7%	3/10 30.0%
		Manual Suturing with 6-0 silk	11/19 57.9%	9/19 47.4%	5/17 29.4%	5/17 29.4%	5/17 29.4%
Tetoron Graft (Control)	5	Manual Suturing with 6-0 silk	1/5 20.0%	0/5 0%			

*** One animal died within 24 hours and 2 dogs were sacrificed within 7 days. They were excluded from the patency rate.

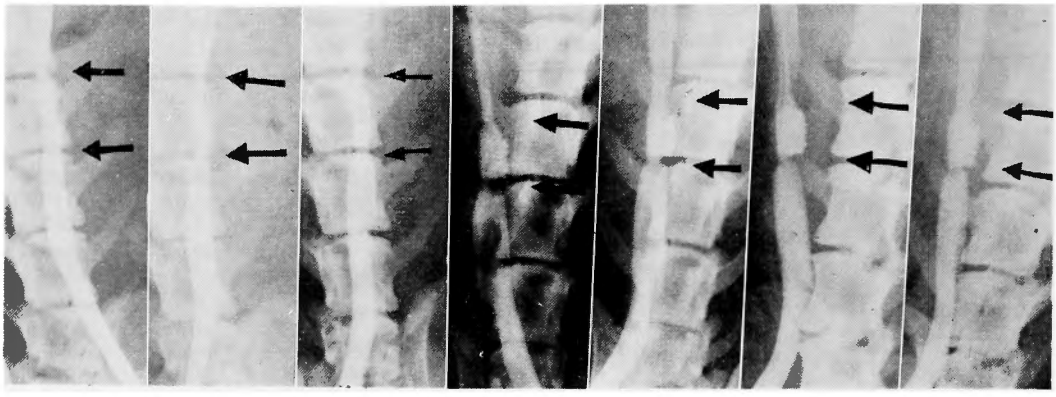
Table 5 Relationship between the Duration of Graft in Abdominal Aorta (Growing Time of Pseudointima) and Patency Rate of Graft

Duration of Graft in Aorta	No.	No. of Graft Patent over 10 wks. in I. V. C.	Patency Rate
22 days 29 days	6	1	16.7%
30 days 39 days	17	6	35.3%
Longer than 40 days	12	8	66.7%

anesthesia at venogram. The remaining 21 dogs being sacrificed at appropriate intervals. The table shows that the patency rate to be 69.0% after 1 week, 55.3% after 2 weeks, and 38.2% after 10 weeks. Apparatus suturing was superior to manual suturing with regard to patency rate. Sixty per cent of grafts anastomosed by the apparatus were patent after 70 days postoperatively. Ten grafts remained patent for longer than 9 months. After placement in the abdominal aorta for various periods the grafts were then inserted into venae cavae. Eight of 12 grafts (66.7%) which had been placed in abdominal aorta for more than 40 days were open after 10 weeks, while only 1 of 6 grafts (16.7%) remained patent in the group of 22 to 29 days (Table 5).

Radiological study revealed little or no constriction or deformity of the grafts shortly after operation. Serial venograms demonstrated a gradual narrowing in entire grafts or at the site of anastomosis in most cases between 5 weeks and approximately 6 months (Fig. 6). However, in certain cases the graft remained completely patent over 1 year with minimal constriction (Fig. 7).

Findings at autopsy were fairly uniform. All the grafts were surrounded by fibrous tissue (Fig. 8). Several grafts in place longer than 180 days showed relatively significant wrinkle or deformity. The internal surface of the patent grafts was lined with a layer of tissue which was reddish-white and swollen shortly after grafting. It became gradually whitish, smooth and glistening pseudointima in about 5 weeks. Grafts removed more than 180 days after insertion were completely covered with white, smooth glistening and relatively thick pseudointima (Fig. 9). In the graft of 555 days, the white smooth glistening pseudointima was circumferentially defective in the center of the graft where fibrin clot was noted



A B C D E F G

Fig. 6 Serial vena cavograms of dog No. 324. Stenosis at the suture lines is minimal shortly after grafting. Gradual constriction at the suture lines is seen after 6 months.
A: 7 days, B: 13 days, C: 110 days, D: 181 days, E: 283 days, F: 400 days, G: 555 days.

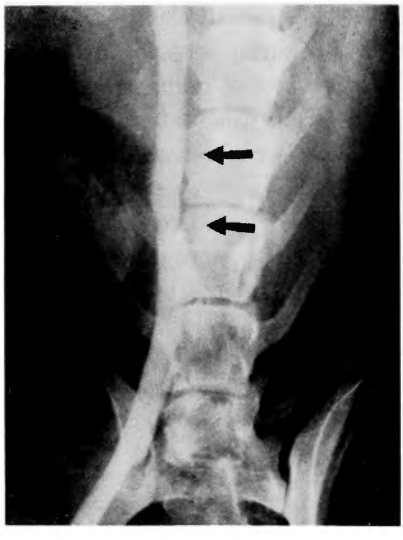
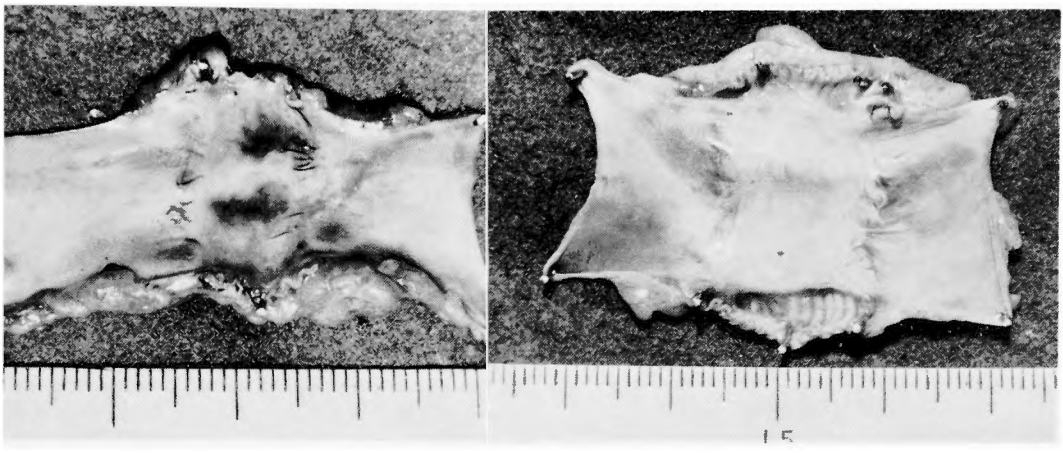


Fig. 7 Vena cavogram of dog No. 345, obtained 395 days after insertion. The graft is of the same caliber as the host vessel and shows minimal constriction at the distal suture line.

Fig. 8 The gross appearance of the graft of dog No. 340, 481 days after insertion. The graft is surrounded by connective tissue.



A B

Fig. 9 A. Graft of dog No. 84, removed 35 days after homologous insertion. Inner surface is covered with white, slightly reddish pseudointima and nylon stitches are visible through the thin pseudointima. B. Graft of dog No. 346, removed 508 days after homologous insertion. Completely covered with smooth, glistening whitish pseudointima. Constriction at the suture lines is minimal.

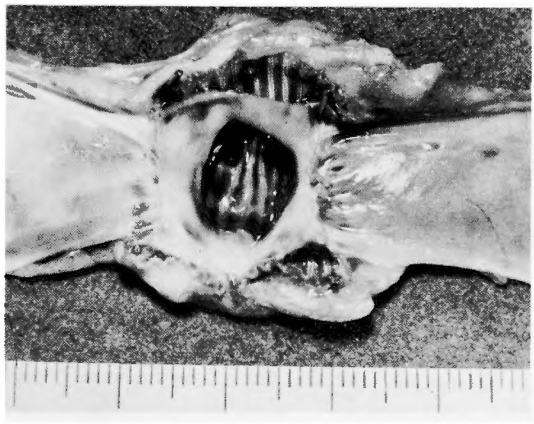


Fig. 10 Graft of dog No. 324, removed 555 days after homologous grafting with Tetoron graft with canine pseudointima. Round defect of pseudointima is seen at the center of the graft where fibrin clot is adhered.

(Fig. 10).

Histologically, 1 day after homologous grafting poorly stained collagen bundles and few fibroblasts were seen. In small areas, the collagenous tissue became homogenous necrotic material. Exudative inflammatory infiltration containing polymorphonuclear leucocytes, a few lymphocytes and some plasma cells was noted around the graft (Fig. 11). After 3 days, laminae of collagenous bundles of implanted pseudointima disappeared and were replaced by eosinophilic homogenous necrotic material in almost all areas. Vacuoles of various sizes were noted in the necrotic material and the accumulation of red blood cells was seen in certain areas. The cellular infiltration of neutrophiles, lymphocytes, and plasma cells was seen both inside and outside the graft. After 6 days, histological appearance was similar to that seen after 3 days but the proliferation of fibroblasts was seen in the host vein near suture lines and invading the necrotized pseudointima (Fig. 12). After 10 days, the graft was surrounded with young connective tissue consisting of remarkably numerous long fibroblasts, collagen fibers and some red blood cells. Several long spindle-shaped fibroblasts invaded through the graft mesh and were replacing the necrotized material (Fig. 13). After 14 days, replacement of necrotic material with connective tissue cells was much advanced. Foreign body giant cells were seen near the graft. After 20 days, the graft was completely covered with connective tissue comprised of connective tissue cells,

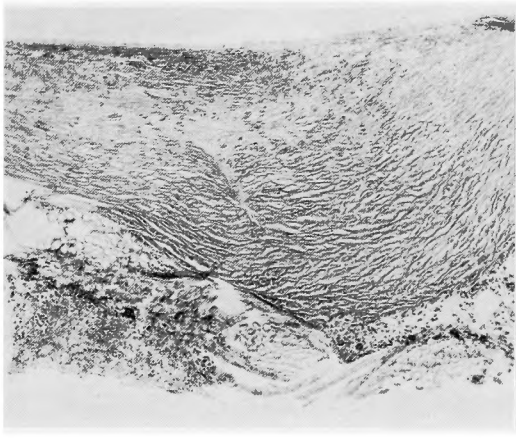


Fig. 11 Section of the graft removed 1 day after homologous grafting with Tetoron graft covered with canine pseudointima. Collagenous bundles are degenerating and exudative inflammation is seen around the graft. ×68

Fig. 12 Section of the graft of dog No. 87, removed 3 days after homologous grafting with Tetoron graft covered with canine pseudointima. Implanted pseudointima became degenerative and necrotic. Hematoxylin and eosin. ×68

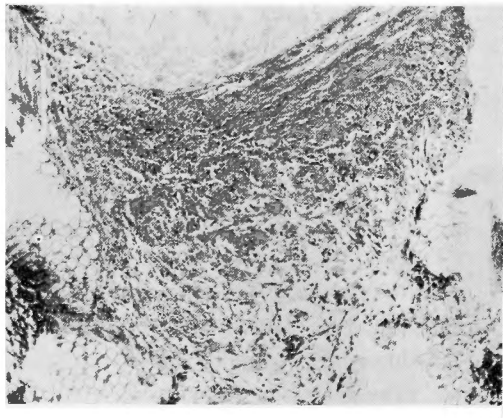


Fig. 13 Section of the graft of dog No. 75, removed 10 days after insertion. Implanted pseudointima became necrotic and cellular infiltration of neutrophils and lymphocytes is noted. Large spindle-shaped fibroblasts have invaded through the graft mesh and are replacing the necrotized material. ×150

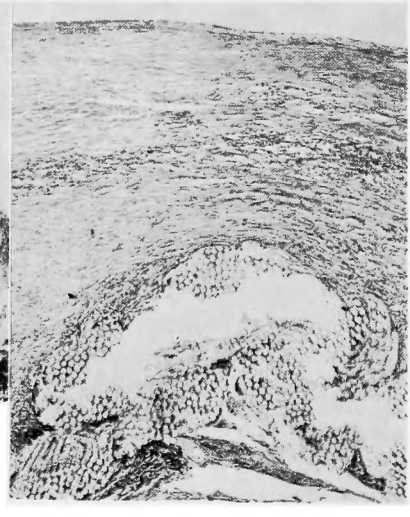


Fig. 14 Section of graft of dog No. 81, removed 20 days after homologous grafting with Tetoron graft covered with canine pseudointima. Necrotized implanted pseudointima has been completely replaced with collagenous connective tissue. Round cells are scattered in the pseudointima. Hematoxylin and eosin ×68

collagenous fibers and several capillaries. The fibroblasts were densely seen near the graft and infiltration of round cells was noted in the midportion of the pseudointima (Fig. 14). After 28 days, matured collagenous bundles with a few connective tissue cells were arranged longitudinally in the superficial portion and in the deeper portion of the pseudointima there were many round cells and fibroblasts. The collagenous bundles of pseudointima appeared to be incorporated into the adjacent venous wall. After 37 days, the graft was covered with matured connective tissue superficially and with young connective tissue nearer the graft. Pseudointima seen after 51 days was similar to that seen after 37 days. After 88 days, pseudointima was composed of matured collagenous bundles and remarkably few fibroblasts. Cellular infiltration near the graft was not intense (Fig. 15). After 175 days, the graft was covered with relatively thick pseudointima in which matured collagenous bundles were arranged longitudinally in the superficial portion. In the midportion the fibrocollagenous tissue was irregularly arranged and was poorly stained. Many capillaries were scattered about and the most striking feature was a lymphocytic infiltration in the mid and deeper portion. After 374 days, almost all collagen bundles were hyalinized superficially and well incorporated into the host venous wall. In the deeper portion, young connective tissue with intense round cell infiltration was noted (Fig. 16). After 410 days, in certain areas near the graft collagenous bundles shrunk and became degenerative. Young fibrous tissue invading the graft mesh was replacing the degenerative tissue. Remaining histological appearance was similar to that seen after 374 days (Fig. 17). Grafts removed 480 to 538 days after implantation possessed hyalinized inert collagenous bundles superficially and relatively young connective tissue with round cell infiltration in the deeper portion. No evidence of degeneration or calcification was observed. In the graft of 555 days, pseudointima disappeared in the center of the graft where the fibrin clot adhered to the graft surface. The rest of the graft was covered with matured connective tissue but pseudointima around the defective area was separated from the graft and fibrin clot was formed in the space between the pseudointima and the graft.

Fig. 15 Pseudointima of the graft of dog No. 372, removed 88 days after grafting. Pseudointima consists completely of collagen bundles and a few fibroblasts and is inert. Hematoxylin and eosin ×230

4. A. HETEROLOGOUS VENOUS REPLACEMENT WITH TETORON GRAFT COVERED WITH CANINE PSEUDOINTIMA

a. Method

Twenty nine cats weighing 1.6 to 4.5 kg were used. Either 1 or 2 cats were prepared simultaneously with a donor dog with Tetoron graft in the abdominal aorta. Infra-renal vena cava of the cat was mobilized as described before. Between 2 SATINSKI clamps the vena

Fig. 16 Anastomotic region of the graft of dog No. 352. Hyalinized collagen fibers are inert superficially and well incorporated into the host venous wall. Young collagenous tissue with round cell infiltration is seen in the deeper portion. ↙ Left: graft, Right: host vein. Hematoxylin and eosin ×68

Fig. 17 Section of the graft of dog No. 354, removed 410 days after grafting. Pseudointima comprises hyalinized collagen bundles superficially and collagenous connective tissue in deeper portions where round cell infiltration is noted. Hematoxylin and eosin ×68

cava was either divided or a 5 mm segment excised. The defect of the vena cava was replaced with the Tetoron graft which had been placed in canine abdominal aorta for 30 to 135 days and had become covered with canine pseudointima. The grafts 1.0 to 1.5 cm in length and of 6 to 8 mm internal diameter were used. Anastomosis were performed with an over-and-over continuous suture using No. 6-0 nylon. Despite the disparity in diameter of the graft and host vein, the anastomosis presented little or no difficulty. Bleeding from the anastomotic lines usually stopped after a pack of moist gauze was applied for 1 to 2 minutes. Blood flow appeared to be satisfactory at the conclusion of the operative procedure. Venography was performed in 13 animals at appropriate intervals.

b. Results

Five cats died within 24 hours, probably due to anesthetic errors, 1 cat escaped from the cage on the 7th day. The remaining 23 cats survived in good health and were followed up to 56 days. Eleven grafts were patent for 1 to 32 days but most grafts showed narrowing or stenosis in the entire graft or at the suture lines (Table 6).

Radiological study revealed significant narrowing or constriction in patent grafts (Fig. 18). Abundant collaterals were seen in occluded grafts.

Autopsy revealed that the graft placed longer than 2 weeks was surrounded with connective tissue. The inner surface of patent grafts was covered with swollen whitish yellowish tissue which reduced the lumen of the graft. The graft of cat No. C-1 was completely patent and covered with white pseudointima (Fig. 19). Twelve grafts were found to be occluded: 3 grafts were filled with thrombus, and 9 grafts with yellowish sloughed material (Fig. 20).

Table 6 Summary of Heterologous Venous Grafting with Tetoron Graft Covered with Canine Pseudointima

No.	Cat No.	Size of Graft (mm)	Growing Time of Pseudointima (days)	Time Followed (days)	Patency at Autopsy	Remarks
1	C-1	6×20	90	10	Patent	White pseudointima completely patent
2	C-2	6×20	76			Died of anesthetic
3	C-3	6×20	62	3	Patent	White smooth inner layer, mural thrombi were noted
4	C-4	6×20	62			Died of anesthetic
5	C-5	6×15	106			Died of anesthetic
6	C-6	8×10	135			Died of anesthetic
7	C-7	8×10	135	30	Patent	Lumen was narrowed with yellowish material
8	C-8	8×10	84	-		Escaped from the cage on 7th day
9	C-9	8×10	84	28	Occluded	Filled with yellowish sloughed material
10	C-10	7×10	40	27	Occluded	Yellowish material at suture lines
11	C-11	7×10	40	28	Occluded	Filled with yellowish sloughed material
12	C-12	8×10	70	19	Occluded	Filled with yellowish sloughed material
13	C-13	8×10	70	24	Patent	Lumen was narrowed with swollen yellowish material
14	C-14	8×13	71	24	Occluded	Filled with yellowish sloughed material
15	C-15	8×13	71	50	Occluded	Filled with yellowish sloughed material
16	C-16	8×12	90	56	Occluded	Filled with yellowish sloughed material
17	C-17	8×12	50	45	Occluded	Yellowish material at suture lines, flattening of graft
18	C-18	8×10	73	32	Patent	Slightly swollen white pseudointima
19	C-19	8×10	73	40	Occluded	Yellowish material at suture lines, flattening of graft
20	C-20	8×15	48	17	Occluded	Thrombosis
21	C-21	8×15	48	25	Patent	Narrowed with yellowish material
22	C-22	7×15	52	19	Patent	Narrowed with yellowish material
23	C-23	7×10	52	19	Patent	Stenosis at suture lines
24	C-24	7×13	54	15	Patent	Center of pseudointima slightly swollen and red
25	C-25	7×15	54		-	Died of anesthetic
26	C-26	7×10	30	3	Occluded	Thrombosis
27	C-27	7×15	30	1	Patent	White smooth inner layer
28	C-28	7×15	50	5	Occluded	Thrombosis
29	C-29	7×15	50	8	Patent	Red smooth inner layer

Histologically, in the graft at 1 day, the collagenous bundles of implanted canine pseudointima were slightly swollen and stained poorly. Fibroblasts which were thought to be of canine origin did not stain well and infiltration of lymphocytes and neutrophiles was seen in degenerating pseudointima. Many lymphocytes were also noted outside of the graft and in the adjacent host venous wall (Fig. 21). After 3 days, canine pseudointima became transformed into eosinophilic, homogenous, necrotic material in which several vacuoles were present. Polymorphonuclear leucocytes, lymphocytes and plasma cells were scattered in the necrotic material. After 8 days, the graft was covered with necrotized pseudointima. In the host venous wall near the suture lines, large round cells, lymphocytes and spindle-shaped fibroblasts were noted and some were invading the adjacent necrotic pseudointima. Some connective tissue cells were invading the graft mesh from the outside of the graft where numerous large round

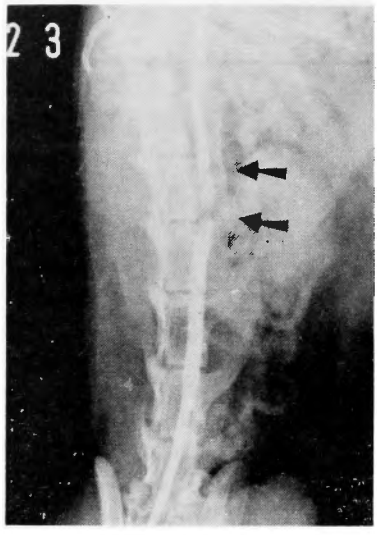


Fig. 18 Venogram of cat No. C-23, taken 19 days after grafting. Significant stenosis at the suture lines is visible.

cells, lymphocytes and some fibroblasts were observed. After 15 days, necrotized material remained in the superficial portion, but it was being replaced with young connective tissue in the deeper portion. Simultaneously, this histological reconstruction proceeded from the adjacent host vein through the suture lines. The graft was surrounded with thick collagenous tissue with some histiocytes and lymphocytes (Fig. 22). After 19 days, replacement of necrotic material with young connective tissue was proceeding gradually from the adjacent host vein and from deeper layer of the pseudointima. After 30 days, near the suture lines, the graft was covered with thick connective tissue. Some collagenous bundles in the superficial portion of this tissue were being incorporated into that of adjacent host venous wall. In the deeper portion of the thick connective tissue, lymphocytes were densely infiltrated. The center of the graft showed necrotic material detached from the graft surface and no evidence of histological reconstruction was noted. After 32 days, the graft was completely covered with relatively thick pseudointima largely comprised of collagenous bundles and abundant round cells. After 40 days, the connective tissue at the suture lines was much thicker and lymphocytic infiltration was significant. At the center of the graft the necrotic material disappeared (Fig. 23). The connective tissue surrounding the graft was thick. After 50 days, the graft was covered with thick collagenous tissue with densely infiltrated lymphocytes.

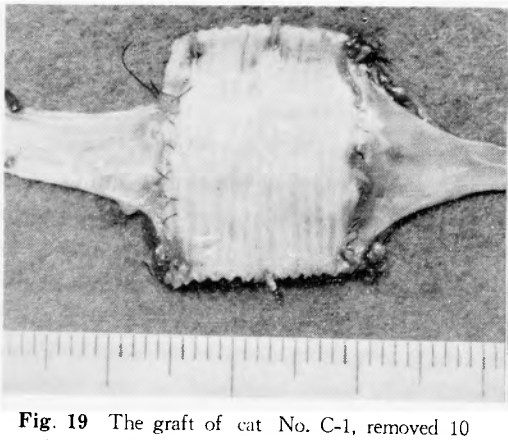


Fig. 19 The graft of cat No. C-1, removed 10 days after heterologous grafting with Tetoron graft covered with canine pseudointima. Completely patent and no evidence of thrombus formation.

Fig. 20 Graft of cat No. C-12, removed 19 days after heterologous grafting. Lumen of the graft is filled with yellowish sloughed material.

Fig. 21 Section of graft of cat No. C-27, removed 1 day after heterologous grafting with Tetoron graft covered with canine pseudointima. Collagenous connective tissue became degenerative and several lymphocytes and neutrophiles are scattered about.
Hematoxylin and eosin ×156

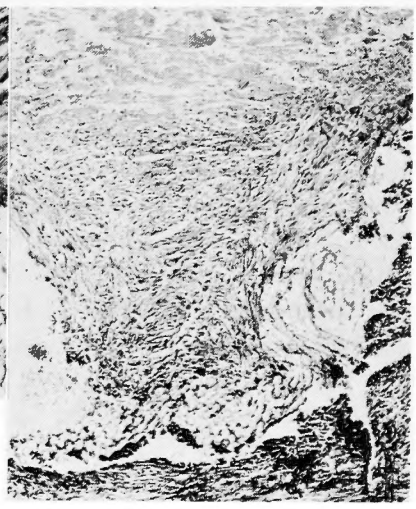


Fig. 22 Section of graft of cat No. C-24, removed 15 days after heterologous grafting with Tetoron graft covered with canine pseudointima. Necrotized canine pseudointima remained superficially but was being replaced with young fibrous connective tissue in the deeper portion.
Hematoxylin and eosin ×91

Fig. 23 Longitudinal section of the graft of cat No. C-19, removed 40 days after grafting. Pseudointima at the suture lines is remarkably thick and it is lost in the center of the graft.
Hematoxylin and eosin ×4

4. B. HETEROLOGOUS PATCH GRAFTING WITH TETORON GRAFT COVERED WITH CANINE PSEUDOINTIMA

a. Method

In 6 cats repair of defect of the inferior vena cava below renal veins was undertaken by patch graft. The patch was cut from crimped woven Tetoron graft which had been placed in the defect of canine abdominal aorta for 91 to 107 days. Through a midline incision, a 5 cm long segemt of inferior vena cava was dissected free. Two SATINSKI clamps were applied and an oval button was excised. The greater diameter of the button removed was oriented longitudinally, parallel with the vessel. The approximate dimensions of the defect and the patch used to repair it were 4×10 mm. The patch was sutured into place with the lesser diameter oriented transversely, comprising about one half of the circumference of the inferior vena cava. Continuous sutures with 6-0 nylon were employed. After removal of clamps, there was a slight constriction at the patch site. The animals were followed for 18 to 54 days.

b. Results

There was 1 anesthetic death on the first postoperative day. Three of the remaining 5 grafts were patent for 18, 31 and 54 days postoperatively (Table 7). The stricture at the site of patch was not evident, but complete pseudointimal coverage of the patch caused a slight reduction in the size of the lumen (Fig. 24). Two grafts resulted in occlusion. The lumen was filled with a yellowish sloughed mass and stricture was noted.

Histologically, the inner surface of the graft at eighteen after days was covered with a layer of tissue which was not as thick as that described before. A homogenous necrotic mass was to a small extent preserved near the graft and in the superficial portion. In the entire area of the tissue, there were numerous cellular infiltration containing large round cells, lymphocytes, fibroblasts, fibrocytes and some red blood cells. Among these cells, collagenous bundles ran longitudinally. Surrounding tissue was thicker than the inner layer, but histological appearance was similar. After 23 days, histological components were the same as that seen after 18 days,

Table 7 Summary of Heterologous Patch Grafting with Tetoron Graft Covered with Canine Pseudointima

No.	Cat No.	Size of Patch (mm)	Growing Time of Pseudointima (days)	Time Followed (days)	Patency at Autopsy	Remarks
1	C-30	3×8	107		–	Died of anesthetic
2	C-31	4×8	107	54	Patent	Smooth glistening pseudointima, minimal constriction
3	C-32	4×8	107	18	Patent	White smooth pseudointima Constriction at graft was noted
4	C-33	4×9	107	22	Occluded	Filled with yellowish material
5	C-34	3×8	56	31	Patent	White pseudointima, significant constriction at graft
6	C-35	3×8	56	36	Occluded	Filled with yellowish material

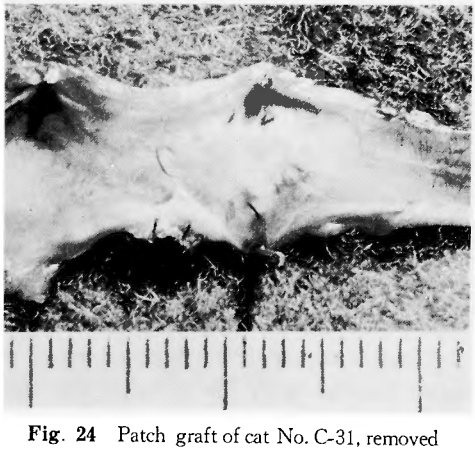


Fig. 24 Patch graft of cat No. C-31, removed 54 days after heterologous grafting with Tetoron graft covered with canine pseudointima. Inner surface of graft is completely covered with whitish smooth pseudointima. Constriction at the suture line is minimal.

Fig. 25 Section of patch graft removed 54 days after implantation. Graft is covered with collagenous connective tissue and collagen bundles are arranged longitudinally in the superficial area. Round cells are densely infiltrated.
Hematoxylin and eosin ×58

but collagen bundles were increased in number. Some collagen bundles were incorporated into the host venous wall. At 54 days, some collagenous bundles were arranged longitudinally on the surface of the pseudointima. Lymphocytes were densely infiltrated in the fibrous tissue (Fig. 25).

III. DISCUSSION

Experimental grafting of the venous system was studied by CARREL and GUTHRIE soon after the turn of the century[6]. This early work lay dormant, however, until the awakening of vascular surgery which followed World War II. Almost every conceivable type of material has been used experimentally and clinically as venous grafts by many investigators[8]. Included in various studies were Vinyon-N[9], Nylon[5], Orlon[5], Ivalon[15)17], Polyethylene[10], Silicone rubber[25], Amylan[25], Dacron[7)9], Teflon[5)14)21], autologous, homologous and heterologous vein and artery[2)17)22)23)30)40], autologous pericardial tube[28], and homologous trachea[35]. However, only a little success has been achieved. Of free graft, only fresh autologous vein has been found to be consistently successful with long-term retention of patency and freedom from constriction and thrombus formation[8]. Unfortunately, the available autologous veins are rarely of adequate caliber for use in the vena cava[1]. Consequently, it is very important to find a suitable venous graft in vascular surgery.

It is generally accepted that the synthetic graft placed in aorta is covered with pseudointima in several weeks and that such a graft remains patent[16)33]. From this evidence the author was encouraged to try to use a synthetic graft of which inner surface was lined with pseudointima[12]. It was further felt that if the transplantation of the pseudointima, with histologically simple structure, were possible in homologous and heterologous animals, it might contribute in solving one of the fundamental problems in organ transplantation and also in developing a new venous graft. The present study was planned to investigate patency rate of the Tetoron graft of which inner surface had been lined with canine pseudointima in the homologous and heterologous infra-renal vena cava and also to study the histological behavior of the pseudointima after transplantation. Tetoron is identical to Dacron and has proved to be a chemically stable, slightly wettable material which incites minimal tissue reaction. Modifying the synthetic graft in vivo by canine pseudointima has, so far as the author can determine, not carried out before. A somewhat similar attempt was performed by SCHILLING et al., who implanted stainless steel wire mesh subcutaneously in the dog and produced fibrocollagenous tubes which were anastomosed to canine abdominal aorta. They reported that the tubes functioned satisfactorily without aneurysmal dilatation[29].

On the surface of this pseudointima of synthetic graft, there was thought to be a layer of cells which were called by such various terms as "pseudoendothelium", "endothelial-like cells", or "flattened cells resembling endothelium". On the nature and origin of these cells, there had been scant information because it was difficult to differentiate endothelial cells from flattened connective tissue cells in conventional longitudinal or cross section of the graft wall. In studies by MEIJNE and by MACKENZIE and LOEWENTHAL, the tissue lining fabric grafts of the aorta has been examined on face after staining with silver nitrate[16)19)20]. The investigators were able to describe and illustrate a layer of flattened cells closely resembling endothelium. There are 3 hypotheses on the origin of graft endothelium: (1)

cellular elements derived from the blood, (2) host endothelium and (3) fibroblasts in the invading granulation tissue[39]. STUMP et al. demonstrated that endothelium can form from the circulating cells in the blood stream[34]. The second hypothesis is strongly supported by MEIJNE, LOEWENTHAL and recently by YONG and his associates[16)20)39]. They thought that graft endothelium is formed by regeneration and extension of adjacent host endothelium because of the histological demonstration of the close resemblance to normal mature host endothelium presented by the regularly arranged graft endothelium cells near suture lines and the appearance of recently regenerated endothelium seen toward the center of the graft. YONG and his associates also reported that there was no evidence to suggest that endothelium was formed by metaplasia of fibroblasts[39]. In the present study the Tetoron graft, removed 22 to 135 days after insertion into canine abdominal aorta, showed coverage of pseudointima macro and microscopically, but the nature and origin of pseudoendothelium was not studied.

Experimental graft replacement of the superior vena cava has been known to be more successful than similar grafting of the infra-renal inferior vena cava in which almost all synthetic grafts became occluded[8]. BOWER et al. used 8 crimped Teflon grafts with only 12.5% patency-rate during 7 days follow up[3]. BRYANT et al. used 4 nylon graft which resulted in complete occlusion within 3 weeks[5]. Collins et al. tried 8 crimped Dacron grafts but they became to occluded within 4 months[7]. In this study the inferior vena cava below renal veins was selected as the most challenging site for graft replacement.

In homologous grafting, 23 of 45 grafts remained patent for various periods up to 555 days, while five control grafts without pseudointima resulted in thrombosis within 10 days. This higher degree of patency rate is thought to be associated with the lining of homologous pseudointima on the internal surface of the graft. Analysed patency rate shows that superior results were obtained in the group with apparatus suturing than in manual suturing. With manual suturing, sutures remain in the lumen as foreign body which is likely to become cause of thrombus formation. Nylon was the superior of the two types of suture material in obtaining high degree of patency, but the reason for this is obscure. MASUOKA reported that the patency rate of graft sutured by nylon was higher than that by silk because nylon induced less tissue reaction than silk[18]. However, in this histological study there was no evidence suggesting that nylon was less tissue reactive than silk.

POOLE et al. reported that complete endothelial coverage of 5.0 to 6.0 cm length of Dacron and Teflon replacing canine arterial defects takes place in 21 to 28 days[26] and STUMPT et al. also found that Dacron grafts are lined with endothelium completely covering the length of a 5.0 to 6.0 cm graft in 21 to 28 days[33]. In present study the Tetoron graft was removed 22 to 135 days after insertion to canine abdominal aorta then transplanted to the homologous vena cava. About four times higher degree of patency rate was obtained by the grafts placed in the aorta for longer than 40 days than that placed for 22 to 29 days. Sufficient pseudoendothelial coverage of Tetoron graft is thought to be the essential factor in successful grafting.

Twenty one grafts became occluded due to thrombosis. All the occlusions occurred within 35 days and 18 occlusions (85.7%) were seen within 14 days. No occlusion was noted thereafter. Similar results were obtained by BRAKHAM and NUNN who reported that the graft patent at 2 months remained patent thereafter[4]. Serial cavograms showed

gradual constriction or narrowing in some grafts until about 180 days, but no occlusion was encountered during the entire follow up of 555 days.

After insertion to the homologous vena cava, implanted canine pseudointima became necrotic and the graft was covered with necrotized sloughed material within about a week. Simultaneously, new fibrous tissue of the second host invaded the graft mesh and necrotized pseudointima was gradually replaced with newly formed pseudointima. This histological process was completed within about 30 days. During this period, until the relining of new pseudointima, the graft is in an unstable condition for maintenance of patency. In this study no occlusion was seen in venograms after 5 weeks.

Soon after the placement of porous synthetic graft in arterial system, fibrin clot adheres to the internal surface of the graft. Simultaneously, granulation tissue containing fibroblasts, fibrocytes, collagen fibers and capillaries begin to invade the graft mesh and the inner surface becomes covered with pseudointima. If hematoma or abscess is present around the graft, the pseudointima is poorly formed. In this study coverage of pseudointima was not sufficient in 3 grafts because of perivascular hematoma. There are several reports that the pseudointimal formation is worse if the porous synthetic graft is wrapped with non-porous sheath[11)31)32)]. From this evidence it is well recognized that the porosity of the synthetic graft plays an important role in the formation of pseudointima and also in the maintenance of patency. However, in a few grafts placed for longer periods pseudointima resulted in degeneration, necrosis and calcification in certain areas. The graft of Dog 324 showed the round defect of once-healed pseudointima in the center of the graft. WESOLOWSKI reported the calcification of the synthetic graft with small size porosity placed in growing pig aorta[36)37)38)]. In the study on healing of synthetic graft, MORIOKA concluded that a porosity of 60μ or more is desirable for better fibroplasia[24)]. The porosity of the Tetoron graft used in the present study is 20 to 30 μ and water porosity is 306.2cc/cm^2/min. at 120 mmHg. It is well known that the pseudointima is nurtured by capillaries through the mesh from outside of the graft. If the porosity is not large enough to permit invasion of capillaries, or the cicatrization of pseudointima reduces interstitial space of the graft in a later stage, pseudointima is likely to result in degeneration, calcification or necrosis. WESOLOWSKI pointed out that water porosity of at least 500 cc/cm^2/min. is necessary to prevent these histological aberration[36)37)38)]. The histological aberration seen in this study is inferred to be related to the small size of porosity of Tetoron graft.

In heterologous grafting, 11 grafts were patent and the longest period of patency was only 32 days. Most occlusions were due to yellowish necrotic material or newly formed thick pseudointima, as well as the small caliber of the graft. With patch grafting, 3 of 5 grafts remained patent for various periods up to 54 days. The graft of cat No. C-31 was completely patent and covered with thin pseudointima and showed minimal constriction. This finding suggests that the heterologous transplantation of pseudointima is not completely hopeless. Taxonomically, dog and cat are very distant, and immunological reaction after heterologous transplantation of canine pseudointima is intense. If the pseudointima was transplanted between two kinds of animals which are closely related, or some method is available to suppress the intense immunological reaction, more satisfactory results might be obtained, and the application of this type of graft would become clinically feasible.

IV. SUMMARY AND CONCLUSIONS

Crimped woven Tetoron graft, which had been placed in canine abdominal aorta and covered with pseudointima, was inserted into the homologous (dog) and heterologous (cat) infra-renal vena cava.

1. 90 Tetoron grafts, 6 to 10 mm in inner diameter and 4 to 5 cm in length, were placed in the canine abdominal aorta for various periods of 22 to 135 days. Seventy two grafts were found to be patent, completely covered with smooth, fairly transparent pseudointima. The remaining 18 grafts were not available as venous grafts because of thrombosis, insufficient coverage of pseudointima or death of animals due to distemper. Thrombosis was seen in higher degree in the graft with smaller caliber.

2. Infra-renal venae cavae of 45 dogs were replaced with Tetoron graft covered with homologous pseudointima. One animal died of anesthetic. Twenty three grafts remained patent for various periods up to 555 days. Ten grafts were patent for longer than 9 months. In analysis of patency-rate, higher degree of patency was obtained in the group with apparatus suturing. In manual suturing, sutures remain in the lumen of the graft as foreign body which is likely cause thrombus formation. Five control grafts without pseudointima became occluded within 10 days because of thrombosis. The higher degree of patency is thought to be associated with the use of the graft covered with homologous pseudointima. Twenty one grafts resulted in occlusion because of thrombosis within 35 days; no occlusion was seen thereafter. Histologically, implanted pseudointima became necrotic and was gradually replaced with newly formed pseudointima in the second host within about 30 days. In a few grafts placed for longer periods, degeneration of the pseudointima was encountered. These changes were felt to be due to the small size of porosity of the graft.

3. Heterologous grafting with Tetoron graft covered with canine pseudointima was undertaken in 29 cats and in another 6 cats patch grafting with same material was carried out. Five animals died and 1 cat escaped from the cage. Eleven grafts were patent for up to 32 days, but were remarkably stenotic. Twelve grafts became occluded : in 3 cases due to thrombus, and in 9 cases the grafts were filled with yellowish sloughed material. Histological findings were qualitatively the same as that in homologous grafting, but cell infiltration was more intense and newly formed pseudointima was thicker. In patch grafting, 3 of 5 grafts remained patent. One case was found to be completely patent for 54 days.

Taxonomically, dog and cat are distant and immunological reaction after heterologous transplantation of canine pseudointima is intense. The patency of the patch graft of 54 days indicates that the heterologous grafting is not completely hopeless. If two kinds of animals which are closely related are used, or some method is available to suppress the intense tissue reaction, more satisfactory results would be obtained and applying the graft clinically would become possible.

* Tetoron graft : Chemically identical to Dacron graft.
Manufactured by Nakao Filter Co. Ltd. Osaka, Japan

** Urokolin : Sodium acetyzoate (Sodium-3-acetylamino-2,4,6-triiodobenzoate)
Manufactured by Daiichi Pharmaceutical Co. Ltd. Tokyo, Japan

ACKNOWLEDGEMENT

The author gratefully acknowledges the valuable advice and instruction of Prof. KIYOSHI INOKUCHI, Second Department of Surgery, Prof. KENZO TANAKA, Department of Pathology, Kyushu University Faculty of Medicine and skilled surgical assistance of the staff of the cardiovascular research group, Second Department of Surgery, Kyushu University Faculty of Medicine.

This study was presented at Second and third Annual Meeting of Japanese Society of Artificial Organ and Tissue, July, 1964 & July, 1965, and 65th Annual Meeting of Japan Surgical Society, April, 1965.

REFERENCES

1) Benvenuto, R., Rodman, F. B. S., Gilmlur, J., Philips, A. F., and Callaghan, J.: Composite venous grafts for replacement of the superior vena cava. Arch. Surg., **84** : 570, 1962.
2) Blum, L., Medl, W. T., and Keefer, F. B. S.: Aortic homograft substitution for the postrenal inferior vena cava. Arch. Surg., **72** : 567, 1956.
3) Bower, R., Fredericci, V., and Howard, J. M.: Continuing studies of replacement of segments of the venous system, Surg., **47** : 132, 1960.
4) Bradham, R. R., and Nunn, D. B.: Autogenous venous grafts and Teflon grafts as small vessel prostheses. Arch. Surg., **81** : 136, 1960.
5) Bryant, M. F., Lazenby, W. D., and Howard, J. M.: Experimental replacement of short segment of veins. Arch. Surg., **76** : 289, 1958.
6) Carrel, A., and Guthrie, C. C.: Uniterminal and biterminal venous transplantation. Surg. Gynec. Obst., **2** : 266, 1906.
7) Collins, H. A., Burrus, G., and DeBakey, M. E.: Experimental evaluation of grafts in the canine inferior vena cava. Am. J. Surg., **99** : 40, 1960.
8) Dale, W. A., and Scott, H. W.: Grafts of the venous system. Surg., **55** : 52, 1963.
9) DeMetz, A., Phillips, L., Habif, D. V., and Jacobson, J. H.: Use of fibrinolysin in experimental inferior vena caval replacement. Arch. Surg., **83** : 883, 1961.
10) Egdahl, R. H., Hume, D. M., and Schlang, H. A.: Plastic venous prostheses. Surg. Forum, **5** : 235, 1955.
11) Harris, E. J.: Pliable plastic aortic grafts. Arch. Surg., **71** : 449, 1955.
12) Inokuchi K., and Ono, K.: Venous replacement with synthetic graft covered with canine pseudointima. Lancet, **7361** : 700, 1964.
13) Inokuchi, K.: A new type of vessel-suturing apparatus. Arch. Surg., **77** : 954, 1958.
14) Jensen, N. K., Garamella, J. J., Schmidt, W. R., and Hoffman, G. L.: Vena caval replacement in man by Teflon graft. A case report. J. Thorac. Cardiov. Surg., **44** : 56, 1962.
15) Jones, T. W., Stevenson, J. K., Jesseph, J. E., and Harkins, J. N.: A critical evaluation of polyvinyl sponge (Ivalon) as a vascular and tissue substitute. Ann. Surg., **24** : 401, 1958.
16) Mackenzie, D. C., and Loewenthal, J.: Endothelial growth in nylon vascular grafts. Brit. J. Surg., **48** : 212, 1960.
17) MacLean, L. D., Phibbs, C. M., Flom, R. S., and Brainard, J. B.: Replacement of vital veins: A comparative experimental study. Ann. Surg., **149** : 549, 1959.
18) Masuoka, S.: Study of superior vena caval replacement. J. Jap. Thorac. Surg., **10** : 30, 1962.
19) Meijne, N. G.: Endothelial growth in nylon vascular prostheses. Arch. chir. Neerl., **41** : 11, 1959.
20) Meijne, N. G.: The neo-intima in vascular prostheses. J. Cardiov. Surg., **5** : 15, 1965.
21) Moore, T. C., Teramoto, S., and Heimburger, I. L.: Successful use of Teflon grafts for superior vena caval replacement. Surg. Gynec. Obst., **111** : 475, 1960.
22) Moore, T. C., Teramoto, S., Heimburger, I. L.: Superior vena caval replacement. Use of fresh homografts of superior vena cava. J. Thorac. Surg., **42** : 376, 1961.
23) Moore, T. C., and Riberi, A.: Superior vena caval replacement, 111 successful use of fresh autogenous aorta. Surg. **44** : 898, 1958.
24) Morioka, K.: Structure of healing of synthetic grafts. J. Jap. Surg. Soc., **66** : 410, 1965.
25) Ohara, I., and Sakai, T.: Transplantation of the large venous system with various blood vessel substitutes. Surg., **42** : 928, 1957.
26) Poole, J. C. F., Sabiston, D. C., Florey, H. W., and Allison, D. M.: Growth of endothelium in arterial

prosthetic grafts and following endarterectomy. Surg. Forum, **13** : 225, 1962.
27) Riberi, A., and Moore, T. C.: Superior vena caval replacement. Experimental use of alcohol-preserved heterografts of bovine aorta. J. Thorac. Surg., **38** : 171, 1959.
28) Riberi, A., Moore, T. C.: Superior vena caval replacement. 1 Unsuitability of free tubes of autogenous pericardium. Arch. Surg., **76** : 384, 1958.
29) Schilling, J. A., Shurley, H. M., Joel, W., White, B. N., Bradford, R. H.: Abdominal arotic grafts: Use of in vivo structured autologous and homologous fibrocollagenous tubes. Ann. Surg., **159** : 819, 1964.
30) Scott. A. E., Horsley, J. S., and Villavicencio, J. L., Warren, R.: Replacement of venous defects by venous autografts. Arch. Surg., **80** : 119, 1960.
31) Self. M. M.: The use of braded nylon tubes for aortic replacement. Ann. Surg., **142** : 836, 1955.
32) Shumacker, H. B., King. H.: The use of pliable plastic tubes as aortic substitutes in man. Surg. Gynec. Obst., **99** : 287, 1954.
33) Stump, M. M., Jordan, G. L., DeBakey, M. E., and Halpert, B. : The endothelial lining of homografts and Dacron prostheses. Am. J. Path., **40** : 487, 1962.
34) Stump, M. M., Jordan, G. L., DeBakey, M. E., and Halpert, B. : Endothelium growth from circulating blood on isolated intravascular Dacron hub. Am. J. Path., **43** : 361, 1963.
35) Todd, R. S., Sive, E. B., DeJode, L. R., Danese, C. and Howard, J. M.: Replacement of segment of the venous system. Arch. Surg., **87** : 998, 1963.
36) Wesolowski, S. A.: The healing of vascular prostheses. Surg., **57** : 319, 1965.
37) Wesolowski, S. A., Fries, C. C., and Sawyer, P. N.: The compound prosthetic vascular graft. 16th Ann. Meeting. The Society for Vascular Surg. (U. S. A.) 1962.
38) Wesolowski, S. A., Fries, C. C., Domingo, R. T., and Liebig, W. J.: The compound prosthetic vascular graft: A pathologic survey. Surg., **53** : 19, 1963.
39) Yong, N. K., Kinmonth, J. B., and Taylor, G. M.: The endothelial lining of vascular grafts. Surg. Gynec. Obst., **117** : 305, 1963.
40) Yong, N. K., Klein, N., and Moore, T. C.: Superior vena caval replacement. Experimental use of fresh autologous vein-grafts. Brit. J. Surg., **51** : 374, 1964.

和文抄録

犬血管仮性内膜付着合成血管による同種及び異種静脈移植の研究

九州大学医学部第2外科学教室（指導：井口　潔教授）

大学院学生　小　野　慶　治

最近の血管外科におけるめざましい進歩にもかかわらず，静脈移植は自家静脈片以外に適当な移植片がなく未解決な分野として残されている．

さて動脈に移植された合成代用血管が数週後に血管仮性内膜により被われ，以後閉塞しにくい事実に著者は着目し，新しい静脈移植片の開発を目的として，この仮性内膜付着代用血管による同種及び異種静脈移植の研究を行なつた．

内径6～10mm，長さ4～5cmの平織テトロン代用血管を雑種犬90頭の腹部大動脈に井口式血管吻合器により挿入し，これを22～135日後に取り出した．72例は合成血管内面が仮性内膜で覆われて完全な状態で開存しており，これらは静脈移植片として用いられた．残り18例は血栓性閉塞，ジステンパー死，仮性内膜不完全生着等の為に使用されなかつた．

雑種犬45頭の腎下部下大静脈に同種仮性内膜付着合成血管を移植した．吻合は井口式血管吻合器及び6－0 Nylon，6－0 Silk による手縫い連続縫合により行なつた．

1例は麻酔死を来したが，44例中23例が最長555日間開存した．9ヵ月以上開存したものは10例みられた．仮性内膜付着のない対照群が全例10日以内に血栓性閉塞に陥つた事より，この高い開存率は合成血管内面に付着する仮性内膜によつてもたらされたものと考える．吻合法別に開存率をみると，器械吻合によるものが最も成績が優れており，更に充分に仮性内膜の成育付着した合成血管を移植した例に高い開存率が認められた．

組織学的には，移植された仮性内膜は変性壊死に陥り，遂次宿主からの線維膠原組織により置換されて新たな仮性内膜が完成する．いつたん仮性内膜により覆われれば移植片は安定化して閉塞しにくくなるが，しかし長期間経過したものの中には，仮性内膜の変性，壊死，石灰化などの異常組織像がみられた．合成血管の Porosity が充分に大きくない場合や，又は仮性内膜の瘢痕化により Porosity が更に小さくなれば仮性内膜を栄養する外部よりの毛細血管の侵入が不充分で循環障害を来たし，異常組織像が起きるものと考えられる．

異種移植は猫29頭の腎下部下大静脈に，犬血管仮性内膜付着合成血管を移植し，そのうち5例が麻酔の失敗により死亡し，1例が逃亡した．残り23例中11例は最長32日間開存したが狭窄の傾向がきわめて強くみられた．閉塞した12例中3例は血栓により，9例は黄色壊死様物質で満されていた．

組織学的に同種移植の場合と質的には同じであるが細胞浸潤及び壊死組織の置換反応が激烈で，新生された仮性内膜もきわめて厚く，更に猫の静脈径が小さい事と相俟つて閉塞し易いものと考えられる．

パッチ移植は5例中3例が開存し，そのうち1例は平滑な薄い仮性内膜で被覆されて54日間満足すべき状態で開存していた．この例は仮性内膜付着合成血管による異種静脈移植は全く悲観的なものではない事を示唆している．

犬，猫は動物分類学上離れた位置にあり，犬，猫の間で仮性内膜の移植を行なえば強い組織反応がみられる．もし分類学上近い二つの動物が用いられ，更に何らかの免疫反応抑制法が得られれば，仮性内膜付着合成血管による異種静脈移植においても満足すべき結果が得られ，最終的にはこの静脈移植片の臨床応用への可能性も充分に考えられる．